Management of Inoperable Cancer of the Breast

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EARLY clinical diagnosis of mammary cancer is seldom easy and the record of cures among those cases considered operable is anything but encouraging. It is apparent that doctors are obliged to deal with a large group of patients for whom some program of palliative management must be carried out. Care of the patient with an inoperable or metastastic lesion is a challenge which has to be met on the basis of the individual case. Following routine rules seldom leads to the best results.

HORMONES

The role of hormones in the genesis and control of neoplastic disease is but vaguely understood. It has been shown that estrogens produce mammary carcinoma in some strains of mice. It has been conclusively shown that estrogens inhibit the growth and spread of carcinoma of the human prostate in certain instances. Both androgens and estrogens have been used in the treatment of carcinoma of the human breast. Until recently the reports of results of such treatment appearing in the literature have been widely different and in some cases confusing. More recent analyses of series of cases so treated indicate how a favorable selection of patients may be made and more or less predictable results obtained.

A fairly large series of cases of advanced carcinoma of the breast has been treated with hormones by English investigators and recently this method has been tried at the Memorial Hospital in New York. Reports seem to agree on one or two points. First, that there is a favorable response in perhaps 40 per cent of cases, particularly in those patients well past the menopause and over 60 years of age. There also is evidence that in young women, and particularly in those around 40 years of age, estrogenic hormone may accelerate the progress of the disease. This is interesting in view of an analysis of 5,000 cases of carcinoma of the breast made by Adair which shows that the peak incidence of cancer of the breast is at 45 years and that another peak occurs at the age of 60. Much remains to be learned about this method of management by hormones. Evidence at present tends to show that the androgenic hormones are of more value in treating carcinoma of the breast in women. With effective doses of estrogen, uterine bleeding, sometimes of a serious nature, was produced in approximately 50 per cent of the cases treated.

Many of the early failures with androgens were probably due to inadequate dosage. Adair has stated that 100 mg. intramuscularly three times a week for a period of eight to ten weeks and totalling up to 3,000 mg. was necessary for effective results. He frankly admits that final conclusions as to the exact dosage and the duration of treatment are not established. The high cost of testosterone propionate hampers the general use of this agent. It appears at this time that the most striking results of the use of testosterone therapy are in those cases where the involvement is of the skeletal tissues. In such cases the improvement frequently is not only clinically patent but demonstrable by x-ray. Associated with testosterone therapy there is a rise in the serum alkaline phosphatase and a diminution in the blood calcium level. These are indications of repair in skeletal tissue. How long improvement which follows androgen therapy will endure is not known, but two of the cases enumerated by Adair have been living for a period of nearly two years free of symptoms after commencing treatment.

It appears that only a small percentage of improvement can be anticipated when cancer involves such tissues as liver, lung, brain, and skin. Present indications are that testosterone is superior to x-ray therapy for bony metastases. Advocates of the use of testosterone as an adjunct in operable carcinoma of the breast and as follow-up prophylaxis in cases apparently successfully operated upon, are coming forward. Experimentation on cancer of other organs such as ovary, uterus, adrenal, testicle, and thyroid, is adding information which is helpful in delineating the effects of this method of treatment. It must be borne in mind that there are a number of very striking side effects which are produced by testosterone therapy in metastatic breast cancer. Some of these are beneficial, some definitely detrimental, and others of a dubious nature. There seems to be nearly always a gain of weight and a sense of well-being sometimes amounting almost to euphoria, in most of these patients. On the debit side are the signs and symptoms of masculinization evidenced by masculine hair distribution, the development of a deep voice, and enlargement of the clitoris, and frequently the appearance of acne not unlike that seen in adolescent boys. Nearly all investigators and experimentors with this agent have noted an increased libido in the treated individuals.

ANALGESIC AGENTS

The effect of analgesic agents on pain is an important consideration in the management of inoperable cancer. Pain is a subjective experience and hard to measure quantitatively. However, there have been one or two methods developed in the pharmacology laboratories for the quantitative measurements of the thresholds of pain perception. One of the best known and perhaps the most reliable is the use of a rheostat-controlled light shining on the blackened skin. Pain is produced by heat in the area so lighted.

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By varying the degree of heat, and with it the pain, the effectiveness of analgesic agents in raising the pain threshold can be measured. Using the response to morphine as a standard and taking the analgesic potency of it as 100, it was found that the potency of aspirin was 35, of alcohol 40, and demerol and dilaudid 105. It was also noted that placebos raised the threshold by the factor 45 in certain instances. This of course tends to minimize the value of any quantitative measurement, but we are all familiar with the fact that if no anxiety exists or if the subject is preoccupied at the time of the test, pain is better tolerated and sometimes even ignored by the same individual whose threshold is lowered if he is anxious, worried, or bored. It was also noted that alcohol was very prompt in its analgesic effect, that when it was given in conjunction with aspirin the effect lasted over a longer period of time, and that the maximal effect was obtained with 30 cc. of alcohol and 0.3 gm. of aspirin.

There is at present no known ideal analgesic substance, and most of them have untoward side effects, such as nausea, depression, constipation, or addiction. It also seems that euphoria and analgesia go hand in hand. For many years morphine has been the basic standard of values. It has a relatively long action and a relatively high euphoric effect. It is more effective against steady than intermittent pain and a greater dosage of it is required to control existing pain than when it is to prevent anticipated pain. The effect of dilaudid, a derivative of morphine, is of shorter duration and it has a less somnifacient and probably less nauseating and constipating effect than the parent drug. Euphoric effects of dilaudid are a little less, but addiction seems to be about the same as for morphine. The drug can be tolerated by some individuals who are intolerant to morphine. Pantopon, a mixture of the alkaloids of opium, is about the same as morphine in action and in the effects and side effects it produces. Codeine is weaker, less nauseating and constipating than morphine, and it seems to be less likely to cause addiction, true addicts shunning it because it does not have the euphoria-producing properties of morphine.

Analgesia is produced by a widely different group of chemicals, and it is impossible to predict from chemical structure whether or not a substance will have pain-relieving properties. Demerol is a substance which illustrates the case in point. It is related to atropine and was discovered in searching for atropine substitutes. It is, however, narcotic in action and has analgesic plus spasmolytic and sedative action. The period of its action is somewhat shorter than that of morphine. It does not produce constipation. It produces less euphoria, and addiction to it is a matter of debate at present. Where spasm is a factor in the production of pain, it has special values.

The discussion of the relief of intractable pain would not be complete without mention of the intraspinal use of ammonium salts. In carefully selected cases where nerve roots of lower segments are involved, this has appeared to give good results and is worthy of further trial by more clinicians. Judovich and his co-workers in Philadelphia advocate its use, using four mg. of ammonium chloride or sulphate, adjusted to a pH of 7.2 administered in 50 cc. of spinal fluid without the use of previous spinal anesthesia. They report the incidence of more pain for a brief period followed by varying degrees of satisfactory relief.

A few cases of bowel and bladder complications following use of it have been reported.

A choice of the various narcotic and analgesic substances is largely an individual one both as regards the physician and the patient. The possibility of addiction in individuals who have hopeless carcinoma with pain should be no deterrent to the effective use of opiates. Alleviation of suffering from this disease should be the principal consideration.

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